

## **REMARKS**

### **1. Amendments to the Claims**

Claim 19 is amended. Claim 19 is supported by the working examples in the Specification wherein an anti-CD81 monoclonal antibody, 2F7, was used.

Claim 32 is amended to recite that “the mammal in need thereof is a mammal suffering from IBD associated with shortening of the intestinal length.” Support for this amendment is found in the Specification at page 101, 5<sup>th</sup> line from the bottom to page 102, Table 3.

No new matter has been added.

### **2. Indefiniteness Rejection**

The Examiner rejects claim 19 for reciting the “biological activity of CD81.” Applicants have amended claim 19, deleting the “biological activity of CD81.” Applicants also point out that Example 5 of the Specification discloses the pharmacological effects of an anti-CD81 antibody could improve the IBD mouse associated with shortening of intestinal length (see Table 3). Thus, the rejection is moot in light of the Amendment. Applicants request that the Examiner withdraw the rejection.

The Examiner rejects claim 32 for reciting “In which the administration of anti-CD81 antibody is associated with the lengthening of the colon of said mammal.” The Examiner states that it is not clear that the antibody results in the “lengthening of the colon.” Applicants point out the data on page 101, line 14 to page 102, line 1 and Table 3 of the Specification discussing the data regarding the lengthening of the colon in mice in a colitis animal model after administration of the anti-CD81 antibody.

### **3. Written Description Rejection**

The Examiner rejects claims 19-20, and 31-32 as lacking written description. The Examiner states that Applicant "is not in possession of any anti-CD81 antibody which blocks a biological activity of CD81 that would treat IBD."

The Examiner cites US 2002/0192748 (hereinafter '748) as teaching that among anti-CD81 antibodies 2F7, Eat 1 and Eat 2 recognizing different epitopes on the CD81 protein, Eat 1 and 2F7 have different effects on astrocyte cell cycle. Applicants submit that '748 is silent about the relationship between CD81 and/or particular anti-CD81 antibodies and inflammation. '748 only discloses the effect of anti-CD81 antibodies on astrocyte cell-cycle in the presence of neurons. Applicants point out that the effects on astrocyte cell cycle do not necessarily correspond to the effect of the respective anti-CD81 antibodies on *inflammatory cells* and IBD.

Applicants submit the Declaration of Mr. Takamasa Watanabe with experimental data showing the effect of the antibodies disclosed in '748 (2F7, Eat I, and Eat II) on the mouse IBD model used in the originally filed Specification. As evident from the Watanabe Declaration, all three anti-CD81 antibodies were equally useful for the treatment of IBD and the treatment of IBD associated with shortened intestinal length. Applicants submit that the data show that Applicants were in possession of a method for improving or treating inflammatory bowel disease by administering an anti-CD81 antibody which blocks a biological activity of CD81 at the time of filing. Thus, Applicants request that the Examiner withdraw the rejection.

### **4. § 102(b) Rejection**

The Examiner rejects claims 19-20 and 32 as anticipated by U.S. Patent 6,423,501 or alternatively WO 98/2564748. Applicants point out that WO 98/2564748 was filed claiming priority to U.S. Applications 60/032,963 and 08/954,279 which matured into U.S. Patent 6,423,501. Thus, hereinafter "'501" refers to both WO 98/25647 and U.S. 6,423,501.

Although the Examiner alleged that the prior art reference discloses a method for treating an inflammatory condition in a mammal comprising administering to the mammal an effective amount of an agent which blocks a biological activity of CD81, '501 fails to effectively show that an anti-CD81 antibody can be used for the treatment or improvement of IBD. Please note that the amended claim 19 does not have the expression "which blocks a biological activity of CD81." Therefore, what claim 19 recites is the administration of the anti-CD81 antibody for the treatment of IBD per se.

Furthermore, Applicants submit that though '501 lists using the antibodies of Fleming to treat IBD, IBD is one of over 20 possible conditions found in that single paragraph. Thus, one of skill is given no direction as to whether the antibodies inhibiting CD-81 cell mediated signal transduction are intended to increase or decrease any mechanisms or effects of IBD, or if they would work at all.

Moreover, the experimental results of '501 are not meaningful in light of a treatment of IBD. '501 discloses that anti-CD81 antibody 5D1 and 1A12 inhibited *in vitro* mast cell degranulation using the RBL-2H3 cell line ('501 col. 19, lines 27-30), as well as *in vivo* IgE mediated mast cell degranulation using the passive cutaneous anaphalixis (PCA) reaction in rat. ('501, col. 11, line 54 to col. 12, line 11). Those results support that anti-CD81 antibody can inhibit FcγRI-induced mast cell degranulation and therefore, is useful for the treatment of an allergy. Although '501 discloses that an agent which induces CD81 mediated signal transduction is useful for the treatment of inflammatory responses associated with disorders associated with disorders such as IBD, '501 fails to show the effect of the agent which induces CD81 mediated signal transduction or the effect of an anti-CD81 antibody on conditions associated with IBD.

PCA is a well known procedure to screen agents for the treatment of type I hypersensitivity or allergy. (See attached, Cruse, Atlas of Immunology, 1999, pages 225-234). On page 233, col. 2, line 15 from the bottom of the page to page 234, col. 1, line 2, the passive cutaneous anaphylaxis (PCA) is explained as an *in vivo* test for type I immediate hypersensitivity. There

have been an enormous number of agents that were evaluated as positive in the PCA test and developed as anti-allergic agents. As far as Applicants know, none of them has been marketed as a treatment for of IBD, even to date. If an agent was positive in the PCA test or useful for the treatment of an allergy, the art would not expect that the agent is useful for the treatment of IBD.

As is discussed in the background art section of the original Specification, there was no satisfactory pharmacotherapy for IBD at the filing date. The situation has not been changed yet. The J. Clin. Gastroenterol., is a review of the drugs for the treatment of IBD. (See attached, Katz, J. Clin. Gastroenterol. Vol. 41, 2007, pages 799-809). Many drugs are discussed in this article, but no anti-allergy drugs are listed. No satisfactory treatment for IBD has yet been developed even as of late 2007.

Accordingly, '501 does not disclose the treatment of IBD with an anti-CD81 antibody in any meaningful way and therefore the art would not expect to use an anti-CD81 antibody for treatment of IBD.

#### **5. Obviousness over '501 and Boismenu and Owens**

Claims 19-20 and 31-32 have been rejected as being obvious over '501 and Boismenu et al. and Owens et al.

As discussed above, '501 only teaches those skilled in the art how to treat allergic reactions and does not at all suggest how any agents described therein would affect IBD. Boismenu and Owens do not teach anything about treating IBD, so no combination of the references would teach the use of an anti-CD81 antibody for the treatment of IBD. Therefore, reconsideration and withdrawal of the rejection are requested.

Conclusion

Pursuant to 37 C.F.R. §§ 1.17 and 1.136(a), Applicant(s) respectfully petition(s) for a two (2) month extension of time for filing a reply in connection with the present application, and the required fee of \$490.00 is attached hereto.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Mark J. Nuell, Ph.D. Reg. No. 36,623 at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

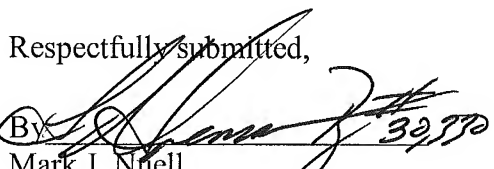
If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.14; particularly, extension of time fees.

Dated: November 17, 2008

Respectfully submitted,

Attachments: Declaration

Cruse, Atlas of Immunology  
Katz, J. Clin. Gastroenterol.  
41:799-809 (2007)

  
Mark J. Nuell

Registration No.: 36,623  
BIRCH, STEWART, KOLASCH & BIRCH, LLP  
12770 High Bluff Drive  
Suite 260  
San Diego, California 92130  
(858) 792-8855  
Attorney for Applicant